

# VII THE SKIN AND APPENDAGES



## GOLDBERGER AND THE MAL DE LA ROSA\*

When Goethe crossed the Alps from Austria into Italy in 1786, he made many observations on pellagrins, recording in his journal:

*I know little, if anything, pleasing to say about the people. As soon as the sun rose over the Brenner paths in the Alps I noticed a decided change in their appearance, and especially displeasing to me was the brownish tan color of the women. Their features indicated misery, and the children were just as pitiful to behold; the men were little better, though their general features were regular and good. . . . I believe the cause of this sickly condition is found in the continued use of Turkish and heath corn.*

In 1735 Casal announced that pellagra was a malady caused by food, and for nearly two centuries a group called *zeists* held the belief that intoxication of poisons in Indian corn caused pellagra. In 1905 Sabmon proposed a different etiology, claiming that pellagra was an insect-borne disease, similar to sleeping sickness, malaria, and yellow fever, leading to a second group called *anti-zeists*. Although pellagra was almost two centuries old in Europe, the question of etiology was still unanswered in 1908 when pellagra was noted to be alarmingly prevalent in southern parts of the United States, particularly in prisons and orphanages. In the report of the distinguished Thompson-McFadden Commission in 1914, this conclusion was reached: "Pellagra is in all probability a specific infectious disease communicable from person to person by means at present unknown." Such was the situation when the U.S. Public Health Service appointed one of its members, Joseph Goldberger, to work on the problem.

\**Mal de la Rosa* is a Spanish term for pellagra, meaning "sickness of the rose."

What is remarkable about Goldberger's achievement is not only that he determined the general cause of pellagra but that he did so with brilliant method.

Already highly regarded for his research on infectious diseases, Goldberger confessed to his wife on receiving this assignment at age 40, "I have never faced anything with greater reluctance" (M.F. Goldberger, 1956). He knew nothing about pellagra and had never seen a case before he began to visit pellagrins in orphanages, insane asylums, prisons, and hospitals throughout the South. A colleague of his wrote that "Goldberger with a new problem was emotionally the boy with a new pair of skates and intellectually Sherlock Holmes with a new murder mystery" (Parsons, 1931).

Goldberger made two distinct observations quickly: (1) that the attendants of pellagrins never got pellagra; and (2) that orphans age 6 through 12 years suffered overwhelmingly from pellagra. With the first observation he considered the disease noncontagious. The second observation led him to believe that it was of dietary etiology, because orphans under age 6 got a large quantity of milk, and orphans over age 12 obtained a better supply of meat. By improving the diet of orphans he noted recovery from pellagra and no recurrence, drawing the conclusion that "pellagra may be prevented by appropriate diet without alteration in the environment, hygienic or sanitary" (Goldberger, Waring, and Willets, 1915).

Goldberger sought to prove his theory by an experiment at a Mississippi penitentiary. In exchange for their pardon, 11 convicts volunteered to eat a pellagra-producing diet. Goldberger's report follows:

*The diet given them consisted of biscuits, fried mush, grits and brown gravy, syrup, corn bread, cabbage, sweet potatoes, rice, collards, and coffee with sugar. All components of the dietary [sic] were of the best quality and were properly cooked.*

*Although the occurrence of nervous symptoms and gastro-intestinal disturbances was noted early, it was not until . . . about five months after the beginning of the restricted diet, that the skin symptoms so characteristic of pellagra began to develop. The symptoms are considered as typical, every precaution being taken to make sure they were not caused by any other disease. The convicts upon whom the experiment was being made, as well as twenty other convicts who were selected as controls, were kept under continuous medical surveillance. No cases of pellagra developed in camp, excepting among those men who were on the restricted diet. The experimenters have, therefore, drawn the conclusion that pellagra has been caused in at least six of eleven volunteers as a result of the one-sided diet on which they subsisted. (U.S. Public Health Service, 1915)*

In spite of the evidence, many physicians remained unconvinced of pellagra's dietary etiology. Goldberger went on to conduct astonishing experiments on himself and willing associates to rule out the possibility of an infectious origin. His wife wrote this account:

*Secretions were obtained by wiping the nose and naso-pharynx of pellagra patients with a cotton swab. These swabs were transferred at once, rubbing them over the mucosa and naso-pharynx first of Dr. Wheeler by Dr. Goldberger, and then of Dr. Goldberger by Dr. Wheeler. Further experiments took place in that month, and in May and June of 1916. Seven separate groups (twenty men and one woman) swallowed in capsules the most nauseating diabolical concoctions made up of secretions of blood, feces, and urine of pellagra patients. Dr. Goldberger himself was a member of each of these groups. On May 7, 1916, I begged to be one of the volunteers and joined him, Dr. Wheeler, and four other men at the hospital in Spartanburg. The men would not consent to my*

*swallowing the pills, but I was given by hypodermic in the abdomen an injection of the blood of a woman dying of pellagra. Not one of us ever showed, as a result, any symptoms of pellagra. (M.F. Goldberger, 1956)*

Before he died at age 55, Goldberger wrote 47 papers on pellagra. On his deathbed, he received word that Harvard University nominated him for a Nobel Prize for the fifth time unsuccessfully.

—CHARLES STEWART ROBERTS

#### **REFERENCES**

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Dermatologic diagnosis depends so much on accurate and complete description of cutaneous findings that an inexperienced but observant medical student who is careful and complete may discover a critical clue overlooked by a competent but hurried examining physician. In evaluating cutaneous disorders, objective findings from the physician's physical examination and office diagnostic tests are weighted more heavily than the patient's subjective history. An initial brief patient-physician interchange establishes rapport and defines the complaint, but a greater proportion of time should be spent on a Sherlockian physical examination of the entire integument of a new patient.

## Principles of Cutaneous Diagnosis (What to Look for)

At the initial physical examination, all cutaneous abnormalities should be noted, using only appropriate morphologic descriptive terms. Any skin lesion can be described by one of the following generic nouns: macule, papule, plaque, nodule, tumor, vesicle, bulla, pustule, wheal, telangiectasis, comedo, burrow, or cyst. These are the *primary lesions*: the morphologic changes most representative of the pathologic process and the basis of the diagnostic categories of dermatologic disease. Primary lesions are discovered by diligent examination, not by history; they do not represent the first lesions experienced by the patient. When primary lesions have been altered by external factors, *secondary changes* are seen: scale, crust, fissure, erosion, ulcer, excoriation, atrophy, scar. Appropriate adjectives such as color (flesh, white, red, purple, brown), surface (smooth, rough), and feel (soft, firm, tender) can be added to the primary and secondary terms to evoke an accurate image in the minds of those reading the database. Note that an "accurate image" does not imply a diagnosis, only generic descriptive terminology.

The examiner should avoid at all costs the temptation to jump to a diagnostic conclusion too rapidly, for many unrelated skin conditions share generic morphologic similarities. A nevus to one examiner may be a seborrheic keratosis or melanoma to another. (The correct and accurate term in this case might be 5 mm brown papule.) The initial history is purposely short because a misleading story can blind even an experienced examiner to significant physical findings that are not consistent with what he or she expects. Before any dermatologic diagnosis is considered, a complete description of skin lesions must establish: (1) primary lesion morphology, (2) arrangement or configuration of lesions, and (3) distribution on anatomic sites. Dermatologic diagnoses should not be made until the physical examination is complete and all the cutaneous findings can be evaluated together (Chapters 105, 106).

When examining patients without overt dermatologic problems, the examiner should always note skin, hair, and

nail abnormalities, as well as lesions such as scars, pigmentation, or moles (nevi) that may be peripheral to the chief complaint but important to the patient's medical evaluation.

## History

The patient should be greeted with a reassuring handshake; the physician should initially assess the patient's general habitus, dress, and emotional state. Brief questioning should establish the duration and location of the cutaneous problem, and what change has brought the patient to the physician at this time. The patient's age, occupation, state of health, and current medications should be determined.

At this point, the physician should explain that questioning will continue with the examination of the skin and that it will be necessary for the patient to undress and drape for a thorough skin examination. The physician should then excuse himself or herself from the room, giving the patient an examination gown and privacy for undressing. In the course of the physical examination, the patient should be asked to point out examples of new lesions and describe what he or she has done to treat the skin.

After the physical examination is complete, further significant details of the history may be elicited from the patient. The patient may be allowed to dress at this point if other examiners will not be participating in the evaluation. Relevant questioning depends to a great extent on the physical findings (Chapter 104).

## Physical Examination

Table 103.1 lists equipment needed for the skin examination. A good source of natural light, a transparent piece of plastic (or double thickness of glass slides) for diascopic

**Table 103.1**  
Equipment Used for the Dermatologic Examination

Good source of natural light
Transparent piece of plastic (or double thickness of glass slides)
Penlight
Gloves
Magnifying glass
For diagnostic tests:
Wood's light
#15 scalpel blade
Microscope slides
Coverslips
20% KOH solution
Mineral (or immersion) oil
Gram's stain
Microscope (10×, 40×)



examination, a penlight for examining the mouth, gloves, and a magnifying glass are helpful adjuncts for the cutaneous examination (Chapter 109). In addition, it may be useful to have a Wood's light for better evaluation of certain pigmented lesions. A nearby laboratory with a microscope should be set up with potassium hydroxide and Gram's stain solutions for use if indicated (Chapter 109).

The steps of the skin examination are presented in Table 103.2. The patient is seated on the examination table in an open-back gown as the examiner enters, washes and dries hands in the patient's presence, if possible. Washing one's hands *before* conducting the physical examination not only assures the patient that he or she will not be the recipient of someone else's "germs" but also decreases the feeling of rejection the patient may perceive if the physician washes up immediately *after* the examination. Physician-patient contact is an important physical and psychologic aspect of the cutaneous examination. It is virtually impossible to transmit infections by contact with dry skin surfaces, so the examiner should not feel uneasy when palpating dry or scaly lesions. However, gloves should routinely be worn when touching mucus membranes, genitalia, moist lesions, and open wounds.

### Hands and Arms

Take the patient's hands and inspect for color and symmetry; then palpate for elasticity, suppleness, and degree of hydration. Examine the palms for scaling or papular eruptions. Note the presence of verrucae, or periungual telangiectasia which may indicate collagen vascular disease. The dorsae of the hands are subject to lifelong sun exposure and indicate the patient's risk for skin cancers on other sun-exposed areas.

The nail examination may give clues to the diagnosis of a number of systemic disorders and should be approached in an orderly manner including the nail fold, lunula, nail bed, hyponychium, and nail plate (Chapter 108).

While inspecting for lesions, the examiner should rub his or her hands along the patient's arms to assess the texture of the skin. Fine-textured, soft skin with ecchymoses may indicate corticosteroid excess, either endogenous overproduction or overuse of topicals. A firm but gentle skin pinch over the outside elbow or forearm will help to determine skin turgor as the pinched fold springs back or remains tented. Examine forearms and antecubital fossae for rashes or scarring.

### Head and Neck

Inspect the skin of the face, noting the degree of wrinkling and freckling, presence of scaling in the nasolabial folds and eyebrows, and pigmented or nonpigmented papules or nodules. Include eyelids, ears, nose, and lips. Have the patient open the mouth and examine mucous membranes of the buccal cavity, gingivae, and tongue. Rub fingertips lightly over the forehead, nose, malar area, and ear pinnae (sun-exposed areas) for the sandpapery feel of actinic keratoses. If keratoses are present, look carefully for pearly translucent telangiectatic nodules indicating basal cell carcinoma.

Inspect the anterior neck, then the right and left lateral neck and behind each ear. Note the presence of scaling or darkening, and palpate skin tags, nevi, and keratoses.

Inspect eyebrows, facial hair (if present), scalp margins,

**Table 103.2**

Sequence for Examination of the Skin

*Patient seated on examining table in open-back gown*

1. Examiner washes hands and dries them.
2. Facing patient, take patient's hands and inspect palms and dorsae of hands.
3. Inspect fingernails.
4. Rub patient's arms for texture and pinch skin for turgor over elbow or forearm.
5. Inspect skin of face, including eyelids, ears, nose, and lips.
6. Look in mouth, examine mucous membranes in oral cavity, tongue.
7. Rub fingertips over forehead, nose, malar area, ear pinnae (sun-exposed areas).
8. Inspect anterior neck, then lateral neck and behind ears.
9. Inspect eyebrows, facial hair (if present), scalp margins, hair and scalp.

*Patient turns to lie on examining table*

10. Unfasten patient gown and inspect back, noting nevi or other lesions.
11. Palpate skin of back and subcutaneous lesions, if present.
12. Inspect gluteal cleft and perianal area.
13. Inspect posterior thighs and lower extremities.

*Patient turns to lie supine on examining table with arms raised*

14. Lower gown to uncover chest (by halves, if patient is female).
15. Pinch palpate infraclavicular area to assess skin turgor.
16. Inspect nipples, inframammary folds, and pannicular folds.
17. Examine axillae, re-cover chest with gown.
18. Raise gown to expose lower abdomen, covering legs with sheet.
19. Wearing gloves, inspect and palpate inguinal folds.
20. Examine genitalia, using stirrups if necessary.
21. Re-cover patient with gown and inspect anterior aspect of lower extremities.

*Patient sits up on examining table and extends legs*

22. Inspect plantar and dorsal surfaces of feet, toeweb, and toenails.

and scalp. Examine the lateral eyebrows, which may thicken and fill in toward the scalp as an early sign of hirsutism or be lost altogether in other systemic disorders. Note lesions in hairy areas that the patient cannot examine easily, and scaling that may indicate seborrhea or psoriasis. Note hair texture, length, color, and abnormalities in growth pattern (Chapter 107). Also note the pattern and distribution of hair over the body during the rest of the physical examination.

### Posterior Torso

Have the patient turn to lie prone (face down) on the examining table and unfasten the top of the examination gown to inspect the back. Examine and note pigmented and flesh-colored papules or other lesions, such as scaly plaques. Palpate the thick skin of the back for subcutaneous lesions, such as lipomas or cysts, which may not be visible.

While the patient is prone, examine the gluteal cleft and perianal area. Part the buttocks and inspect the intertriginous skin for maceration, scaling, or perianal verrucae. If lesions are found, note them for closer examination during the gloved genital examination (see below). Re-cover the patient's back and buttocks with the gown, but do not tie at the neck. Moving down, inspect the posterior thighs and

lower extremities for lesions that the patient may not have seen; note rashes in the popliteal fossae.

#### *Anterior Torso*

Have the patient turn to lie supine on the examining table. Lower the unfastened gown to uncover the chest and free the arms: for modesty in female patients, this can easily be done one arm and quadrant at a time, with practice. Gently pinch palpate the infraclavicular area to assess skin turgor and hydration state. Inspect nipples, inframammary folds, and pannicular folds. Examine axillae for nodules, skin tags, or darkening.

Re-cover the chest with the top of the gown and cover the legs with a sheet, then raise the bottom of the gown to expose the lower abdomen. Put on gloves and inspect the inguinal folds, noting erythema or scaling and palpating for nodes. Examine pubic hair for nits and look for ulcerations anywhere on the genitalia. Note urethral discharge or genital warts; ask the uncircumcised male patient to retract his foreskin; inspect the glans penis. Raise the scrotum for perineal inspection. (Examining table stirrups afford better visualization of the genitalia and perianal area in either sex.) With gloves, examine the female vulva, including the major and minor labia. Look for pigmented plaques on the labia majora, and for papillomas at the posterior introitus.

Inspect anterior thighs, knees, and pretibial areas. Symmetrical lesions may be seen on the knees in psoriasis, and thyroid disease and diabetes produce characteristic pretibial changes. Note edema or pigmentary changes around the ankles.

Ask the patient to sit up on the examining table with

each leg extended in turn and inspect the plantar and dorsal surfaces of the feet, the toenails, the toeweb (especially the third and fourth spaces, which are especially susceptible to fungal infections.) Note lesions, scaling, and erythema.

#### **Summary**

Distracting conversation should be avoided during the cutaneous examination, but valuable information may be gained by occasional questions about the lesions encountered. In contrast to the examination of other organ systems, patients often actively participate in looking at their skin with the examiner. This makes it easier for the examiner to inquire whether there has been a change in a particular lesion: a mirror may be used to help the patient consider a facial lesion, for example. Commenting aloud that a given area appears normal or mentioning the presence of benign-appearing lesions or scars lessens patient apprehension and helps the examiner recall findings to be noted on the written database.

New patients with skin problems limited to a small area may resist disrobing for a complete skin examination, but they are generally willing to cooperate when the examiner explains that it is important to perform a thorough baseline examination so that later changes might be more accurately assessed. Explain that systemic disorders are sometimes detected by subtle skin signs and that skin cancers are often asymptomatic. A friendly but relentless positive attitude on the part of the examiner will gradually overcome modesty, and an inquiry about lesions that have worried the patient or the patient's spouse will often lead to voluntary unbuttoning.